Seizure 19 (2010) 475–478

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Value of 3.0 T MR imaging in refractory partial epilepsy and negative 1.5 T MRI

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ARTICLE INFO

Article history:
Received 1 February 2010
Accepted 1 July 2010

Keywords:
Focal epilepsy
Refractory epilepsy
Magnetic resonance imaging
3.0 T vs 1.5 T

ABSTRACT

Background: High-field 3.0 T MR scanners provide an improved signal-to-noise ratio which can be translated in higher image resolution, possibly allowing critical detection of subtle epileptogenic lesions missed on standard-field 1.0–1.5 T MRIs. In this study, the authors explore the potential value of re-imaging at 3.0 T patients with refractory partial epilepsy and negative 1.5 T MRI.
Methods: We retrospectively identified all patients with refractory partial epilepsy candidate for surgery who had undergone a 3.0 T MR study after a negative 1.5 T MR study. High-field 3.0 T MRIs were reviewed qualitatively by neuroradiologists experienced in interpreting epilepsy studies with access to clinical information. Relevance and impact on clinical management were assessed by an epileptologist.
Results: Between November 2006 and August 2009, 36 patients with refractory partial epilepsy candidate for surgery underwent 3.0 T MR study after a 1.5 T MR study failed to disclose a relevant epileptogenic lesion. A potential lesion was found only in two patients (5.6%, 95% CI: 1.5–18.1%). Both were found to have hippocampal atrophy congruent with other presurgical localization techniques which resulted in omission of an invasive EEG study and direct passage to surgery.
Conclusions: The frequency of detection of a new lesion by re-imaging at 3.0 T patients with refractory partial epilepsy candidate for surgery was found to be low, but seems to offer the potential of a significant clinical impact for selected patients. This finding needs to be validated in a prospective controlled study.

1. Introduction

Despite the regular introduction of new anticonvulsants on the market, many epileptic patients continue to have drug-resistant seizures. Their best option is often to consider surgery. In the context of epilepsy surgery, the main challenge is finding the precise location of the epileptogenic zone in the brain, in order to remove it and end the seizures. In the presurgical evaluation, MRI (Magnetic resonance imaging) is particularly useful in that aspect as the location of a structural lesion is usually congruent with the epileptogenic zone. Several studies confirm that detection of an epileptogenic lesion on MRI substantially improves the outcome of an epilepsy surgery.[1,2]

The strength of the magnetic field of an MRI scanner is measured in Tesla (T). Many refer to field strengths ≥3.0 T as 'high-field', 1.0–2.0 T as 'standard', and <0.5 T as 'low field'. The vast majority of epilepsy protocol MRI studies are currently performed on a 1.0–1.5 T scanner and include (a) a volume acquisition T1-weighted data set acquired in an oblique coronal orientation and covering the whole brain in 0.9 mm partitions; (b) an oblique coronal spin-echo sequence, with proton density, heavily T2-weighted and FLAIR acquisitions that are orientated perpendicular to the long axis of the hippocampus.[3] Using these conventional acquisitions, abnormalities are detected in ≥80% of patients with refractory temporal lobe epilepsy but in only 50–60% of patients with refractory neocortical epilepsy.[4] High-field 3 T MRIs were approved recently by the *American Food and Drug Administration* (FDA) for clinical use and have been introduced progressively in academic centers over the last few years. High-field MRIs provide an improved signal-to-noise ratio which could theoretically result in higher image resolution, possibly allowing critical detection of subtle epileptogenic lesions missed on standard field MRIs.[5] The question arises whether patients with refractory partial epilepsy and a previously negative 1.5 T MRI should be re-imaged with a 3 T MRI now that these are more popular. We address this issue in this retrospective study.

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doi:10.1016/j.seizure.2010.07.002

2. Methods

We retrospectively identified all refractory partial epilepsy patients candidate for epilepsy surgery in whom a 3.0 T epilepsy protocol MRI was performed between November 2006 and August 2009 because a previous standard field MRI (1.0–1.5 T) had failed to identify a relevant epileptogenic lesion. Patients were eligible if they had undergone a comprehensive presurgical evaluation including a clinical history and examination, long-term video-EEG monitoring for recording of seizures, and at least one epilepsy protocol head-coil standard field (1.0–1.5 T) MRI scan at our center or an affiliated academic center. All standard-field MRIs had been read previously by an unblinded experienced neuroradiologist. The study was approved by our institutional ethics committee with waiver of informed consent.

2.1. MRI

The initial 3.0 T scans were performed at the CRIUGM, a research center affiliated with the University of Montreal on a Siemens Tim TRIO (Siemens AG, Berlin, Germany). The remaining 3.0 T scans were performed at Notre-Dame Hospital when the Achieva Dual 3.0 T system was installed in January 2008 (Philips Medical Systems, Best, Netherlands). All 3.0 T studies included (a) a 3D T1-weighted gradient-echo acquisition of the whole brain (TR/TE, 24/6; flip angle, 25°; field of view, 256 mm × 256 mm; matrix, 256 × 192); (b) axial T2-weighted (TR/TE, 24/6; flip angle, 25°; field of view, 256 mm × 256 mm; matrix, 256 × 192) and FLAIR (TR/TE, 24/6; flip angle, 25°; field of view, 256 mm × 256 mm; matrix, 256 × 192) acquisitions of the whole brain; (c) coronal T2-weighted and FLAIR acquisitions perpendicular to the longitudinal axis of the hippocampus. Intravenous contrast agents were given only if a mass lesion was demonstrated.

2.2. Image review

High-field MRIs were reviewed qualitatively by neuroradiologists experienced in interpreting epilepsy studies and with access to clinical information. If an abnormality was identified on the high-field MRI study, the finding was interpreted by an epileptologist to determine whether the abnormality was relevant to the patient's epileptic condition and if it resulted in a change in clinical management. The localization of each patient's epileptogenic zone was determined based on multimodal analysis of clinical, electrophysiological (scalp EEG, MEG) and functional (PET, SPECT, EEG-fMRI) data. Findings from intracerebral findings, pathological examination of the tissue resected and surgical outcome were also used when available.

3. Results

3.1. Patients

We identified 36 (20 M/16 F; age 13–56 yo/median 31 yo) patients with refractory partial epilepsy candidate for epilepsy surgery whose 1.5 T MRI failed to detect a relevant epileptogenic lesion and who underwent re-imaging at 3.0 T between November 2006 and August 2009. Median interval between the two MRIs was 22.5 months (range 0 day–13 years). Localization of the epileptogenic zone was based on multimodal analysis of clinical, scalp EEG, functional (SPECT and PET) data for all patients. Magnetoencephalography was obtained in 26 subjects and EEG-fMRI in 24 subjects. Additional invasive EEG findings were available for 10 patients. Sixteen had frontal lobe epilepsy, 15 had temporal lobe epilepsy, three had parietal lobe epilepsy and two had occipital lobe epilepsy.

3.2. Standard-field MRI

As determined by our inclusion criteria, standard-field MRI failed to reveal a congruent epileptogenic lesion in all patients. Twenty-five were performed at our institution using our epilepsy protocol. The remaining cases were scanned in other affiliated academic hospitals also benefiting from an epilepsy protocol. Ten patients had unspecific or unrelated brain abnormalities on their 1.5 T MRI: Chiari type I malformation (1), arachnoid cyst (1), small white matter signal abnormalities (4), quadrigeminal plate lipoma (1), mild atrophy (2), or slight malrotation of hippocampus (1) but contralateral to the suspected epileptogenic zone.

3.3. High-field MRI

High-field MRIs were obtained using a 3.0 T Siemens Tim TRIO (Siemens AG, Berlin, Germany) in 11 cases and a Philips Achieva Dual 3T (Philips Medical Systems, Best, Netherlands) in the other 25. High-field imaging identified an abnormality in two out of 36 patients (5.6%) (see Table 1). A mild left hippocampal atrophy was discovered for case 6 whose electroclinical data suggested left mesial temporal lobe epilepsy. A mild right hippocampal atrophy was found for case 13 whose presurgical evaluation suggested right mesial temporal lobe epilepsy. Intervals between standard and high-field MRI studies for both patients were 32 and 10 months, respectively. In light of these findings, it was decided to omit the invasive EEG study in both cases. Patient 13 underwent a right anterior temporal lobectomy with Engel 1 outcome (31 months follow-up) while Patient 6 is waiting to be operated. Of the 10 patients with unspecific or incongruent findings on their 1.5 T MRI, 3.0 T imaging provided no further information. One patient with negative 1.5 T MRI was found to have a small white matter signal abnormality far from and contralateral to the suspected epileptogenic zone.

4. Discussion

Outcome of epilepsy surgery is intimately linked to accurate localization of the epileptogenic zone.[6] Any technique enabling our capacity to detect an underlying pathological substrate is bound to increase our chance to delimit this epileptogenic zone. Introduction in the 1980s of MRI for clinical use has revolutionized the evaluation of partial epilepsy, unveiling previously undetected lesions such as cortical developmental malformations and hippocampal atrophy. This in turn has led to better surgical outcome, reduced need for intracranial EEG studies as well as disclosing a new population of potential candidates for epilepsy surgery. Because numerous studies have shown such a strong correlation between seizure relief and resection of a visible structural lesion, finding evidence for such an epileptogenic lesion has assumed an important role in the presurgical work-up of patients with intractable partial epilepsy.[7]

Most hospitals are equipped with a commercial whole-body magnet operating at 1.0–1.5 T. Several studies have already shown the benefit of dedicated MRI protocols interpreted by experienced neuroradiologists.[8,9] Technological advances have allowed the development of more powerful magnets and 3.0 T MR scanners have been progressively installed worldwide for clinical use over the last few years. A greater magnetic field strength provides a higher signal-to-noise ratio which in turn allows faster imaging for a given resolution or higher resolution for a given imaging time. The obvious implication for epilepsy patients is that higher field MRI has the potential to detect subtle epileptogenic lesions that might have been missed by low-field or standard-field MRI. Formal comparison is however required to confirm improvements in the detection of epileptogenic lesions by 3.0 T scanners over current

Table 1
Summary of clinical and presurgical findings, intracranial EEG results, and surgical outcome.

Patient	Epilepsy	MRI 1.5 T; detected epileptogenic lesion	MRI 1.5 T; non-specific abnormality	MRI 3 T added findings	ICE	Surgery	Outcome (Engel)	F-U (mo)	Pathology
1	R FLE	No		No	No	No			
2	R FLE	No	Small WMSA	No	No	No			
3	Bi-MTLE	No		No	No	No			
4	R FLE	No		No	No	No			
5	R NTLE	Slight malrotation of contra-lateral L hippocampus vs variant		No	No	No			
6	L MTLE	No		Yes (mild L HA)	No	No			
7	Bi-MTLE (L ⋙ R)	Contralateral mild R HA		No	Yes	L ATL	I	3	CA1,3,4 cell loss, gliosis
8	R NTLE	No	Chiari type I	No	No	No			
9	R FLE	No		No	Yes	R F corticectomy	I	2	Pending
10	L NTLE	No		No	No	No			
11	L FLE	No	Small lipoma, small WMSA	No	No	No			
12	L NTLE	No		No	No	No			
13	R MTLE	No		Yes (mild R HA)	No	R ATL	I	22	CA1 cell loss, gliosis
14	R FLE	No	Small WMSA	No	Yes	R F corticectomy	I	23	normal
15	R PLE	No		No	Yes	R P corticectomy	I	22	Cortical dysplasia
16	R FLE	No		No	Yes	R F corticectomy	I	23	Cortical dysplasia
17	L FLE	No		No	No	No			
18	L NTLE	No		No	No	No			
19	R MTLE	Contralateral mild L HA		No	Yes	R SAH	I	24	Not available
20	L NTLE	No		No	No	No			
21	R FLE	No		No	No	No			
22	L FLE	No		No	Yes	L F corticectomy	IV	24	Microdysgenesis
23	R OLE	No		No	Yes	R O corticectomy	I	12	Normal
24	R MTLE	No		No	Yes	R ATL	I	4	CA1, 3, 4 cell loss, gliosis
25	L NTLE	No		No	No	No			
26	L PLE	No		No	No	No			
27	bi-MTLE	No	Small WMSA	No	No	No			
28	L NTLE	No		No	No	No			
29	L FLE	No		No	No	No			
30	R PLE	No		No	No	No			
31	L FLE	No		No (small WMSA)	No	No			
32	R FLE	No	Discrete vermal atrophy	No	No	No			
33	R FLE	No		No	No	No			
34	OLE	No		No	No	No			
35	L FLE	No		No	No	No			
36	R FLE	R HA but suspected EZ is R frontal		No	Yes	No			

Abbreviations: R, right; L, left; NTLE, neocortical temporal lobe epilepsy; MTLE, mesial temporal lobe epilepsy; FLE, frontal lobe epilepsy; PLE, parietal lobe epilepsy; OLE, occipital lobe epilepsy; ICE, intracranial electroencephalogram; HA, hippocampal atrophy; WMSA, white matter signal abnormality; ATL, anterior temporal lobectomy; SAH, selective amygdalo-hippocampectomy; EZ, epileptogenic zone; Engel classification: I, free of impairing seizures; II, rare disabling seizures; III, worthwhile improvement; IV, no worthwhile improvement.

1.5 T clinical scanners as there are certain disadvantages of working at higher field. These include increased susceptibility artefact from magnetic field inhomogeneity in orbitofrontal and temporal brain regions nearing air-filled nasal cavities as well as poorer T1-weighted contrast by convergence of tissue T1 values which may negate the theoretical increase in signal to noise ratio over 1.5 T images.[10,11]

Our study shows that re-imaging non-lesional focal epilepsy patients at 3.0 T provided clinical relevant findings in only two out of 36 patients (5.6%). This estimation is also associated with a substantial uncertainty (95% CI: 1.5–18.1%) related to this small population. Despite this low detection rate, the abnormalities that were found did have an impact on clinical management. Both were found to have mild hippocampal atrophy congruent with other presurgical findings, obviating the need for invasive EEG monitoring. Higher-field imaging also disclosed an unrelated lesion (small white matter signal abnormality) in one case (false positive).

Limited studies have looked at the value of structural imaging at higher field for epilepsy. Volumetrically derived volumes of amygdala and hippocampus from 1.5 and 3.0 T images did not differ in eight healthy subjects[12] and 10 temporal lobe epilepsy patients.[13] Griffiths et al.[5] reported their initial experience of imaging 120 adults with localisation-related epilepsy using MR imaging at 3.0 T (SENSE head coil) but provided no comparison with 1.5 T imaging data. In the only prospective study available, Knake et al.[11] reported that 3.0 T MRI with a custom-made eight-channel flexible receive-only phased array coil resulted in the detection of a new lesion in 15 of 23 (65%) patients with medically intractable focal epilepsy and normal 1.5 T MRI. Unfortunately, the authors were unable to separate the benefits of differences in expertise between radiologists, use of higher field strength, or use of the phased array head coil. Similar dramatic detection rates of new lesions have not been reported since. Phal et al.[14] attempted a formal comparison of standard and high-field structural MRIs for epilepsy by retrospectively reviewing images from 25 patients who underwent both 1.5 T (with transmit-receive single-channel head coil) and 3.0 T (with six-channel SENSE head coil) scanning. MRI at 3.0 T outperformed MRI at 1.5 T for image quality parameters (distortion and artefact, lesion conspicuity, gray–white matter differentiation, and motion). Sub-analyses on the 19 patients with partial epilepsy revealed that lesions were detected in 74% of cases done on 1.5 T MRI compared to 88% at 3.0 T. These findings are however not directly comparable to our series as the

authors included patients regardless of the reason for repeating imaging (such as previously normal or equivocal results at 1.5 T but also lesional follow-up and surgical planning). In fact, only 5 cases out of 19 partial epilepsy patients had a negative 1.5 T MRI. Strandberg et al.[15] reported that 3.0 T (4 channel head coil and parallel imaging) MRI provided new or additional information about structural grey matter abnormalities, compared to reports from 1.0 to 1.5 T MRI, in five (out of 25) patients (20%). In one 1.5 T MRI-negative patient, a malformation of cortical development was identified. In four other patients with unspecific findings (cortical atrophy, heterotopia, increased signal changes after subpial transection) on 1.0 or 1.5 T MRI, malformations of cortical development were identified on 3.0 T MRI. The higher detection rate compared to our findings could possibly be explained by the fact that two of their patients would have been excluded in our study. After removing the patient with heterotopia and the patient with increased signal changes after subpial transection detected at 1.5 T, the detection rate drops to (8.7%). More recently, Zijlmans et al.[16] scanned 37 epileptic patients considered ineligible for surgery based on available presurgical findings using a 1.5 T MR (with an 8-channel phased array SENSE head coil) scanner and a 3.0 T MR scanner (with a similar phased-array head coil). The first experienced neuroradiologist identified 22 lesions on both 1.5 and 3.0 T studies while the second identified 28 lesions on the 1.5 T MR study as opposed to 20 lesions on the 3.0 T MR study. Hence, in total, fewer lesions were surprisingly identified on 3.0 T with phased-array coil than on 1.5 T with phased-array coil. Subanalyses suggested that 3.0 T phased-array coil images might be more liable to detect dysplasias while 1.5 T phased-array coil images were better to detect tissue loss. Although this study imaged a different population (i.e. patients ineligible for surgery and not necessarily nonlesional) than ours and used phased-array coils in both 1.5 and 3.0 T scans (making it impossible to determine the benefit of going from 1.5 to 3.0 T field strengths independent from the contribution of phased array coils), it provides argument that the gain provided by imaging at higher field is not necessarily obvious nor remarkable.

Hence, in response to our question whether re-imaging our nonlesional refractory patients was essential and what benefits it brought them, it would appear that the rate of detection of a new epileptogenic lesion by 3.0 T structural imaging is low (5.6%) though the impact of identifying such a lesion on clinical management was significant. One could advocate that despite this low rate of detection, epilepsy surgery candidates with negative 1.5 T MRI should still be re-imaged at 3.0 T considering it could prevent a costly invasive EEG study with potential risks of infection and haemorrhage as well as improve surgical outcome. However, there is little to support re-imaging at 3.0 T patients with well-controlled partial epilepsy. The frequency of lesions not detected on standard-field MRI is expected to be even lower in this population as malformations of cortical development and hippocampal abnormalities are mostly encountered in refractory patients.

The retrospective nature of our study introduced certain limitations. As in other studies, some standard-field MRIs were performed in other centers where patients were previously followed prior to referral to our institution. Although these centers were affiliated academic centers using epilepsy protocols, small differences in MR systems and acquisitions parameters could result in variable image quality. Furthermore, there might be some differences between neuroradiologists in their expertise with epilepsy MR studies. Finally, an unblinded reader reproduces clinical practice but introduces a certain investigation bias in favor of the 3.0 T. The delay between both 1.5 and 3.0 T MRI was acceptable in our study to prevent introducing a bias that would be related to progressive tissue changes. In any case, a longer delay would have only created a bias in favor of 3.0 T MRI.

With the increasing availability of 3.0 T MR scanners for clinical purposes along with phased-array coil development, more robust data is clearly needed to provide recommendations. A prospective study addressing issues mentioned above is currently underway in our institution in which controls and patients with refractory partial epilepsy with negative 1.5 T MRI will undergo three additional MR studies: 1.5 T with phased-array coils, 3.0 and 3.0 T with phased-array coils. Interpretation of images by two blinded experienced neuroradiologists on two separate occasions, correlation with other presurgical localization technique and intracerebral recordings or pathological examination when available, assessment of impact on clinical management will be performed.

Acknowledgements

The study was funded by the Fonds pour la Recherche en Santé du Québec. The authors would like to thank all patients and their treating neurologists.

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